REMARKS

Non-Compliant Amendment and Patent Term Adjustment

Applicants respectfully disagree with the Examiner's allegation that the Response to Office Action Filed January 6, 2011, was non-compliant. Claims 18 and 19 were relied on as the basis for finding the Response non-compliant. However, claims 18 and 19 were withdrawn and remained in their original form as filed. Thus, the claim identifiers associated with claims 18 and 19 were accurate. Further, the Examiner did not object to or reject claims 18 and 19 in the substantive Office Action of October 6, 2010. Applicants had not noticed the typographical errors in claims 18 and 19, and neither did the Examiner. The response filed January 6, 2011, was fully responsive to the rejections made in the Office Action. Despite the typographical errors in withdrawn claims 18 and 19, their meaning was clear and an objection could have been made by the Examiner is a subsequent Office Action upon their possible rejoinder.

Although Applicants disagree with the Examiner's allegation that the Response filed January 6, 2011, is non-compliant, in the interests of expediting prosecution, Applicants are herewith submitting the instant response amending claims 18 and 19, as suggested by the Examiner. However, Applicants respectfully request that the patent term on a patent issuing from the present application not be reduced as a result of the Examiner's assertion that the Response of January 6, 2011 was non-compliant.

Status of the Claims

Claims 1-19 are pending in the present application. Claim 1 is independent. Claims 2-5, 7, 11-13 and 16-19 are withdrawn from consideration, as being drawn to nonelected subject matter.

Claim 1 has been amended to positively recite method steps, as suggested by the Examiner. Amendments to claim 1 are supported throughout the Specification as filed. See, for example, lines 20-24 on page 21 of the Specification. Claims 18 and 19 have also been amended, as suggested by the Examiner to correct typographical errors. Thus, no new matter has been introduced by way of amendment to the claims.

Reconsideration of this application, as amended, is respectfully requested.

Priority under 35 U.S.C. § 119

Applicants thank the Examiner for acknowledging Applicants' claim for foreign priority under 35 U.S.C. § 119. However, the Examiner has not acknowledged receipt of certified copies of the priority documents.

Applicants respectfully submit that certified copies of the priority documents appear in PAIR. Acknowledgment of receipt of certified copies of the priority documents is respectfully requested in the next Office Action.

Information Disclosure Citations

Applicants thank the Examiner for considering the references cited in the Information Disclosure Statements filed October 18, 2006, and May 12, 2008, and for providing Applicants with initialed copies of the PTO-SB08 forms filed therewith.

Drawings

Applicants thank the Examiner for indicating that the drawings are accepted.

Examiner Interview

Applicants wish to thank the Examiner for the courtesies extended to Applicants' representative during the Interview which was conducted on September 23, 2010. An Examiner Interview Summary was made of record and is an accurate description of the substance of the Interview.

Rejection Under 35 U.S.C. §§ 101 and 112, second paragraph

Claims 1, 6 and 8-10 stand rejected under 35 U.S.C. §§ 101 and 112, second paragraph. This rejection is respectfully traversed.

In the Office Action, it is alleged that claims 1, 6 and 8-10 provide for the use of an index of protein expression without setting forth any steps involved in the method/process making the claims indefinite.

In order to address this rejection, Applicants have amended independent claim 1 to positively recite steps in the claimed method. Specifically claim 1 has been amended to recite assay methods comprising sampling a cancer cell from a cancer tissue and optionally culturing the cancer cell *in vitro*; measuring the expression level of pRB, p16 and/or cyclin E of the cancer

cell; and predicting the cancer cell will be sensitive to the compound based on any one of the recited indices. Claims 6 and 8-10 depend from claim 1 and therefore, after amendment, they also positively recite steps in a method.

Applicants respectfully submit that the claims, as amended, particularly point out and distinctly claim statutory subject matter which Applicants regard as the invention. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 101 and 112, second paragraph, are respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 6, 8-10 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cover, C.M. et al, "Indole-3-carbinol inhibits the expression of cyclin-dependent kinase-6 and induces a G1 cell cycle arrest of human breast cancer cells independent of estrogen receptor signaling," J Biol Chem, February 13, 1998, Vol. 273, No. 7, pages 3838-3847 (hereinafter "Cover") in view of Fukada et al., WO 03/099813 (hereinafter "Fukada"), as evidenced by U.S. Patent Appl. Publ. No. 2006/0009439 serving as an official English translation of Cover. This rejection is respectfully traversed.

Claims 1, 6, 8-10 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sandor, V. et al, "P21-dependent g(1)arrest with downregulation of cyclin D1 and upregulation of cyclin E by the histone deacetylase inhibitor FR901228," Br J Cancer, September 2000, Vol. 83, No. 6, pages 817-825 (hereinafter "Sandor") in view of Fukada. This rejection is respectfully traversed.

The claimed methods predict anticancer (antitumor) activity of an inventive compound based on the expression of cyclin E, pRB and p16 in different types of cancer cells (optionally cultured *in vitro*).

In the Office Action, it is asserted that Cover teaches:

(1) monitoring protein expression of cyclin E and Rb by western blotting, citing page 3840, paragraph 2 and Figures 3 and 4;

(2) the expression level of cyclin E and the amount of pRB increases in cancer cells, citing page 3839, paragraph 3; and

(3) endogenous Rb protein levels are decreased in (I3C)-treated cells causing the cell cycle to stop, citing page 3842, paragraph 3 and page 3846, paragraph 6 and Figure 4.

Further it is asserted in the Office Action that Sandor teaches:

(4) inhibitors of cancer and their mode of action, citing the Title;

(5) treating cancer cells with a compound such as FR901228 and analyzing the effects thereof upon protein expression by western blotting, citing page 818, paragraph 2;

(6) monitoring protein expression levels of cyclin E and Rb by western blotting, citing page 818, paragraph 4; and

(7) the expression level of cyclin E is decreased after cancer cells are exposed to the anticancer drug FR901228 causing growth of the cancer cells to stop, citing the Abstract.

Applicants respectfully disagree with these characterizations of the prior art.

Cover merely discloses that changes in protein levels were detected upon administering the compound I3C to a single cell type, MCF7. Cover is silent regarding predicting anticancer effects of a test drug based on the expression levels of cyclin E, pRB and/or p16 in different cancer cell types without exposure to a compound, as in the claimed invention.

Further, Applicants disagree with the assertions in the Office Action that Cover teaches (2) the expression level of cyclin E and the amount of pRB increases in cancer cells and (3) endogenous Rb protein levels are decreased in (I3C)-treated cells causing the cell cycle to stop. Cover discusses references teaching that up to 45% of human breast cancers show an aberrant expression and/or amplification of cyclin Dl or cyclin E. However, Cover is silent regarding expression levels of pRB in cancer cells. In addition, Cover discloses that cells treated with I3C do not have altered expression of cyclin E, page 3841, right-handed column, line 7 from the bottom and Figure 3. Moreover, Cover only discloses that levels of phosphorylated pRb change after administration of the compound. Thus, Applicants disagree with the assertion in the Office Action that Cover teaches (3) endogenous Rb protein levels are decreased in (I3C)-treated cells causing the cell cycle to stop.

Sandor, like Cover, merely discloses that levels of phosphorylated pRb change after administration of the compound studied, see Figure 3. Thus, Applicants respectfully disagree

with the assertion in the Office Action that Sandor teaches (6) monitoring expression levels of cyclin E and Rb by western blotting. Further, Sandor merely observed changes in expression levels of cyclin E after administration of the compound (Figure 5). Sandor did not teach methods to predict the effectiveness of a compound as an anticancer agent based on specific changes in expression observed without exposing cancer cells to the compound, as in the claimed invention.

Fukuda is merely relied on as teaching the elected species (Compound 2, Formula III).

Cover, Sandor and Fukuda, taken alone or together, do not teach assay methods to predict sensitivity of a cancer cell to a compound represented by formula I comprising assay methods comprising sampling a cancer cell from a cancer tissue and optionally culturing the cancer cell *in vitro*; measuring the expression level of pRB, p16 and/or cyclin E of the cancer cell; and predicting the cancer cell will be sensitive to the compound using any one index of: 1) expression of pRB is reduced; 2) p16 is expressed; 3) expression of cyclin E is enhanced; 4) expression of pRB is reduced and expression of cyclin E is enhanced; or 5) p16 is expressed and expression of cyclin E is enhanced; as in the claimed invention.

In view of the discussion above, Applicants respectfully request that the rejection of claims 1, 6, 8-10 and 14-15 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Stephanie A. Wardwell, PhD, Registration No. 48,025 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: FEB 10 2011

Respectfully submitted,

By GARTH M. DAHLEN
USPTO #43,575

Marc S. Weiner
Registration No.: 32181
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road, Suite 100 East
P.O. Box 747
Falls Church, VA 22040-0747
703-205-8000